Abstract

Crystal Structure of the GpIbα–Thrombin Complex Essential for Platelet Aggregation

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Direct interaction between platelet receptor glycoprotein Ibα (GpIbα) and thrombin is required for platelet aggregation and activation at sites of vascular injury. Abnormal GpIbα–thrombin binding is associated with many pathological conditions, including occlusive arterial thrombosis and bleeding disorders. The crystal structure of the GpIbα–thrombin complex at 2.6 angstrom resolution reveals simultaneous interactions of GpIbα with exosite I of one thrombin molecule, and with exosite II of a second thrombin molecule. In the crystal lattice, the periodic arrangement of GpIbα–thrombin complexes mirrors a scaffold that could serve as a driving force for tight platelet adhesion. The details of these interactions reconcile GpIbα–thrombin binding modes that are presently controversial, highlighting two distinct interfaces that are potential targets for development of novel antithrombotic drugs.